**Supporting Information**

**Experimental and theoretical investigation of GS-441524 using Density Functional Theory, FTIR, Raman, and UV-VIS spectroscopy**

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**Table S1.** B3LYP/6-311++G(d,p) optimized geometry of GS-441524. The X, Y, and Z coordinates are in Å.

|  |  |  |  |
| --- | --- | --- | --- |
| **Atom** | **Χ** | **Υ** | **Ζ** |
| O1 | -3.99344300 | -0.29053800 | 0.54425900 |
| O2 | -1.94438400 | -1.13429000 | 2.04713100 |
| H3 | -1.15577800 | -1.43134100 | 2.51127100 |
| O4 | -1.32467800 | 0.26160700 | -1.21792000 |
| O5 | -1.22164200 | 2.93341800 | -0.03873800 |
| H6 | -0.42728800 | 2.37723900 | -0.12551700 |
| N7 | 5.04280700 | -0.22448000 | 0.11382000 |
| H8 | 5.78756000 | 0.45295700 | 0.16409300 |
| H9 | 5.25857400 | -1.16263900 | -0.17584700 |
| N10 | 1.40667300 | -0.06368100 | -0.04209800 |
| N11 | 3.57686500 | 1.53375800 | 0.32247400 |
| N12 | 1.19668700 | 1.26986600 | 0.16691200 |
| N13 | -2.21423700 | -3.01025600 | -0.94542700 |
| C14 | 2.50672700 | -2.01244100 | -0.29921700 |
| H15 | 3.28583900 | -2.75432600 | -0.37640000 |
| C16 | -1.60499500 | -0.17349700 | 1.07154200 |
| H17 | -0.88426600 | 0.55289700 | 1.45108000 |
| C18 | 2.67594600 | -0.65063400 | -0.07410500 |
| C19 | 3.77226000 | 0.23881300 | 0.11708600 |
| C20 | 1.12687500 | -2.23906500 | -0.41025300 |
| H21 | 0.64267000 | -3.18374800 | -0.59957100 |
| C22 | -2.18366700 | 2.48939500 | -0.97878400 |
| H23 | -1.85012400 | 2.66657500 | -2.00981800 |
| H24 | -3.09040100 | 3.07781200 | -0.81295800 |
| C25 | -2.86645200 | 0.56842200 | 0.60418600 |
| H26 | -3.06381500 | 1.42729000 | 1.25307600 |
| C27 | -1.02823400 | -0.75299700 | -0.26887100 |
| C28 | -1.71760000 | -2.02016800 | -0.62834800 |
| C29 | 0.45426600 | -1.02822400 | -0.24839200 |
| C30 | -2.51493400 | 1.01267900 | -0.82453400 |
| H31 | -3.33539400 | 0.73390600 | -1.49225100 |
| C32 | 2.29626000 | 1.96188000 | 0.33676000 |
| H33 | 2.14089300 | 3.02187500 | 0.50527500 |
| H34 | -3.99557000 | -0.84150700 | 1.33751400 |

**Table S2.** BP86/6-311++G(d,p) optimized geometry of GS-441524. The X, Y, and Z coordinates are in Å.

|  |  |  |  |
| --- | --- | --- | --- |
| **Atom** | **Χ** | **Υ** | **Ζ** |
| O1 | -4.00228600 | -0.29839700 | 0.51768700 |
| O2 | -1.96161700 | -1.10291000 | 2.06425400 |
| H3 | -1.15241500 | -1.46517000 | 2.46284200 |
| O4 | -1.33267300 | 0.26361100 | -1.24200800 |
| O5 | -1.18309100 | 2.92650200 | -0.00270000 |
| H6 | -0.39624400 | 2.33607500 | -0.09754000 |
| N7 | 5.05943600 | -0.24364000 | 0.12549200 |
| H8 | 5.80402400 | 0.44838700 | 0.14610000 |
| H9 | 5.27665800 | -1.18064200 | -0.19499900 |
| N10 | 1.40371300 | -0.06732700 | -0.04534900 |
| N11 | 3.59551900 | 1.53475000 | 0.31066000 |
| N12 | 1.19532300 | 1.27350800 | 0.15112200 |
| N13 | -2.23893700 | -3.02617600 | -0.92900200 |
| C14 | 2.49988700 | -2.03813900 | -0.28654900 |
| H15 | 3.28018300 | -2.79228500 | -0.35451700 |
| C16 | -1.61381100 | -0.15011300 | 1.07082300 |
| H17 | -0.88374700 | 0.58832500 | 1.44072900 |
| C18 | 2.68066900 | -0.66667900 | -0.06953800 |
| C19 | 3.78173600 | 0.22307500 | 0.11517100 |
| C20 | 1.11323600 | -2.25749100 | -0.40133500 |
| H21 | 0.61614100 | -3.20652800 | -0.58739400 |
| C22 | -2.15058000 | 2.51463500 | -0.96335900 |
| H23 | -1.80419100 | 2.69895800 | -1.99987200 |
| H24 | -3.05360600 | 3.12581400 | -0.79650400 |
| C25 | -2.88150300 | 0.58279700 | 0.59363300 |
| H26 | -3.09463900 | 1.44589600 | 1.24998600 |
| C27 | -1.04158000 | -0.74988200 | -0.27223200 |
| C28 | -1.73798100 | -2.02166800 | -0.61287700 |
| C29 | 0.44106300 | -1.03421000 | -0.24879200 |
| C30 | -2.51867100 | 1.03888500 | -0.83208700 |
| H31 | -3.35003900 | 0.78170200 | -1.51144500 |
| C32 | 2.31150200 | 1.96710300 | 0.31907400 |
| H33 | 2.15423000 | 3.03751800 | 0.47843800 |
| H34 | -3.96819400 | -0.87619600 | 1.30425600 |

**Table S3.** CAM-B3LYP/6-311++G(d,p) optimized geometry of GS-441524. The X, Y, and Z coordinates are in Å.

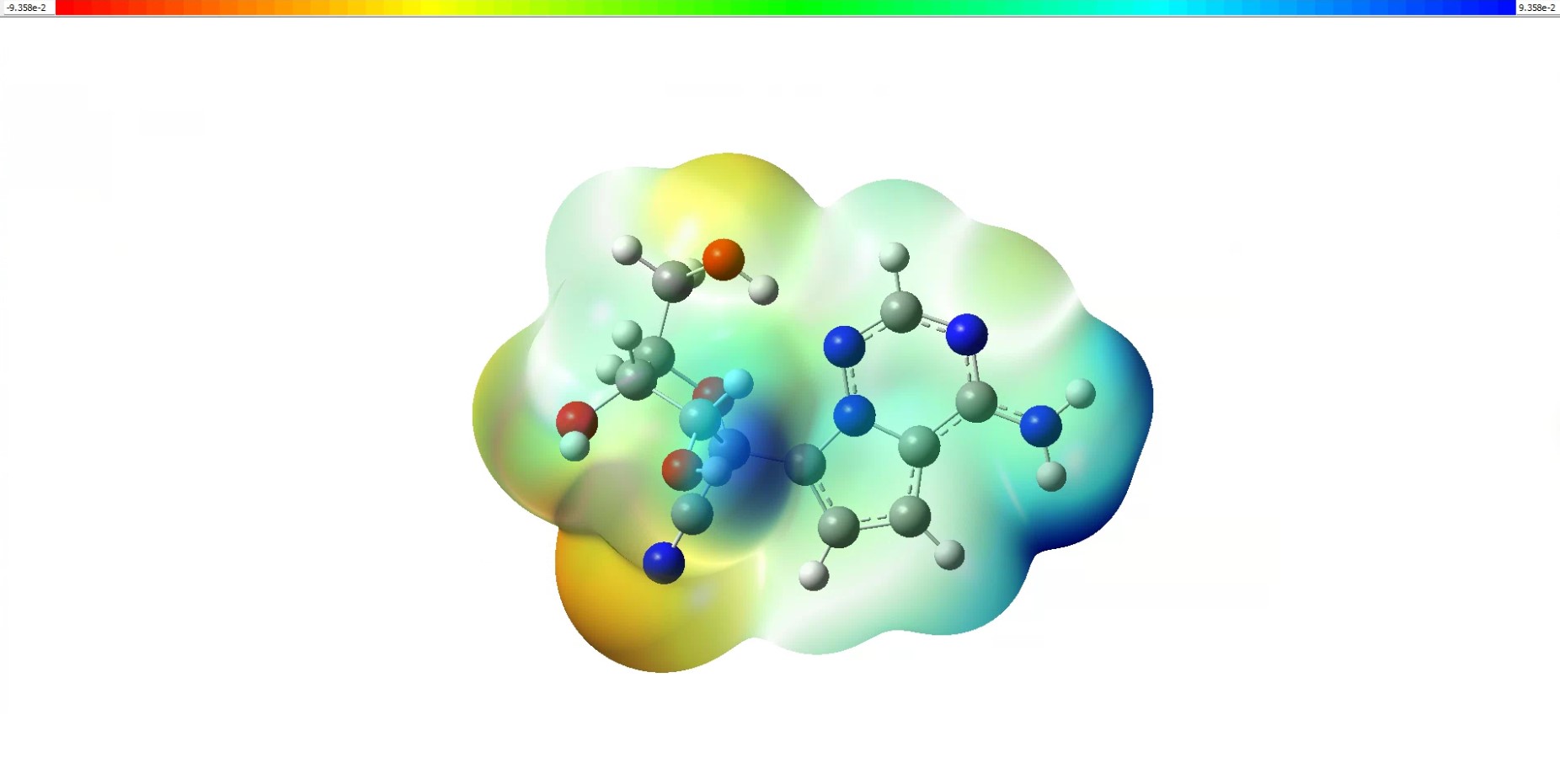
|  |  |  |  |
| --- | --- | --- | --- |
| **Atom** | **Χ** | **Υ** | **Ζ** |
| O1 | -3.96228000 | -0.30067400 | 0.52548100 |
| O2 | -1.93575700 | -1.12350700 | 2.02792500 |
| H3 | -1.15022200 | -1.44697900 | 2.47612300 |
| O4 | -1.31574700 | 0.27210300 | -1.20992600 |
| O5 | -1.19989100 | 2.89899800 | -0.00636100 |
| H6 | -0.40758100 | 2.34357900 | -0.10402900 |
| N7 | 5.01414500 | -0.23439000 | 0.10534100 |
| H8 | 5.76686500 | 0.42793900 | 0.19871500 |
| H9 | 5.22143600 | -1.19346200 | -0.10827800 |
| N10 | 1.39816000 | -0.06597500 | -0.04611100 |
| N11 | 3.56108700 | 1.52204400 | 0.30976500 |
| N12 | 1.19261100 | 1.26529300 | 0.15292400 |
| N13 | -2.21145500 | -2.99031600 | -0.93407800 |
| C14 | 2.48703100 | -2.00797200 | -0.28855500 |
| H15 | 3.26489100 | -2.75071900 | -0.36344000 |
| C16 | -1.59703100 | -0.16333800 | 1.06194300 |
| H17 | -0.87888700 | 0.56390200 | 1.44281800 |
| C18 | 2.65489100 | -0.65224800 | -0.07290900 |
| C19 | 3.75396700 | 0.23516100 | 0.11488200 |
| C20 | 1.10937200 | -2.23187000 | -0.39897000 |
| H21 | 0.62192100 | -3.17535200 | -0.58426900 |
| C22 | -2.15786900 | 2.48916100 | -0.95492200 |
| H23 | -1.81629800 | 2.67911800 | -1.97944000 |
| H24 | -3.05892900 | 3.08259400 | -0.78404400 |
| C25 | -2.85453400 | 0.56965700 | 0.59556900 |
| H26 | -3.06533000 | 1.42314200 | 1.24521000 |
| C27 | -1.02829500 | -0.73784400 | -0.26931400 |
| C28 | -1.72190500 | -2.00096400 | -0.62653600 |
| C29 | 0.44720000 | -1.02362800 | -0.24634100 |
| C30 | -2.49771900 | 1.01962300 | -0.82278100 |
| H31 | -3.31643900 | 0.75006100 | -1.49443900 |
| C32 | 2.28307500 | 1.95390800 | 0.31788000 |
| H33 | 2.13096500 | 3.01501900 | 0.47860400 |
| H34 | -3.95392100 | -0.86868200 | 1.30495100 |

**Table S4.** Vibrational assignment for the experimentally observed FT-IR and Raman wavenumbers (cm-1) and comparison with BP86/6-311++G(d,p) calculations. Relative intensities are denoted by vs (very strong), s (strong), m (medium), m-s (medium to strong), w (weak), vw (very weak), and vr (variable), N/A (not available in the literature). The width of the peak is denoted by b (broad), and sh (sharp). In the case where an assignment can be allocated for two peaks, the second time is written as revised (rev.). Unless noted otherwise, the third column (vibration type) refers to intensities in infrared from the literature [Socrates, 2001], and the fourth column refers to vibration types obtained using the GaussView animations from the theoretical calculations from this work.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Experimental IR | Experimental Raman | Vibration type | Theoretical  IR | Theoretical  Raman |
| 3471 s, sh | - | 3670 - 3580 vr+m-s, b or sh Ο-Η stretching (alcohols) | 3718 vw  stretching C(2')O-H | 3718 m, sh |
| 3425 s, sh | - | 3670 - 3580 vr+m-s, b or sh Ο-Η stretching (alcohols)  3670 - 3580 vr+m-s, b or sh Ο-Η stretching (alcohols) | 3651 vw  stretching C(3')O-H | 3651 m, sh |
| 3334 s, sh | - | 3520 - 3420 m, b Ν-Η asymmetric stretching (primary aromatic amine) | 3636 vw  Ν-Η asym. stretching | 3636 m, sh |
| 3228 m | - | 3420 - 3340 m, b Ν-Η symmetric stretching (primary aromatic amine) | 3505 w, sh  Ν-Η sym. stretching | 3505 m, sh |
| 3186 m, br | - | 3670 - 3580 vr+m-s, b or sh  Ο-Η stretching (alcohols) | 3404 vs, sh  stretching C(5')O-H We note that C(5')O-H makes an H-bond with N-1 of triazine as their H distance from O/N is smaller than 3.5 Å reducing the observed frequency. | 3404 vs, sh |
| 3084 | 3056 | 3100 -3010 m =C-H stretching (pyrrole)  3100 - 3000 m C-H stretching of triazine | 3179 vw  sym. stretching Η-C-C-H of pyrrole ring  3163 vw  asym. stretching Η-C-C-H of pyrrole ring  3108  C-H stretching of triazine | 3179 m, sh  3163 (m, sh)  3108 m, sh |
| 2948 w | 2937 vw | 2990 - 2900 vr+m-w C-H asym. stretching (CH2 in primary alcohols (CH2-ΟΗ))  2980 - 2700 m-s Tetrahydrofurans, multiple peaks | 2993 vw  asym stretching C-H in primary alcohols & C-H stretching of tetrahydrofuran  2990 vw  C-H stretching of tetrahydrofuran | 2993 s, sh  2990 m, sh |
| 2908 w | 2913 vw | 2990 - 2900 vr+w-m C-H asym. stretching (CH2 in primary alcohols (CH2-ΟΗ))  2980 - 2700 m-s Tetrahydrofurans, multiple peaks | 2972 vw  asym. stretching C-H of primary alcohol & C-H stretching of tetrahydrofuran  2950 vw  C-H stretching of tetrahydrofuran | 2972 s, sh  2950 s, sh |
| 2852w | - | 2935 - 2840 vr+w-m C-H sym. stretching of primary alcohols (CH2-ΟΗ)  2980 - 2700 m-s Tetrahydrofurans, multiple peaks | 2913 vw  sym stretching C-H of primary alcohol & C-H stretching of tetrahydrofuran | 2913 s, sh |
| 2763 w  2717 w | - | 2980 - 2700 m-s Tetrahydrofurans, multiple peaks | - | - |
| 2243 vw | 2245 w | 2260 - 2200 vr+ (from vw to vs), sh -CN stretching | 2245 vw  -CN stretching | 2245 s, sh |
| 1658 vs  1610 s | 1664 vw 1605 vw | 1615-1580 (Ν/Α) Ν-Η deformation of ΝΗ2 (in aromatic amines)  1608 m-s C=N stretching of triazine ring [Alrooqi, 2022]  1558 in-plane and totally symmetric stretching of N3C2 and C5C6 in the triazine ring, [Thastum Bach99] | 1599 s, sh  Ν-Η deformation (scissoring) of aromatic ΝΗ2  in-plane stretching of triazine ring or heterocyclic base | 1599 vw |
| 1539 s shoulder at  1518 | 1541 w  1519 w  1479 vs shoulder at 1453 | 1625-1430 vr+m-s C=C stretching of aromatic rings | 1489 w, b  stretching of aromatic heterocyclic rings | 1489 s, sh |
| 1475 s, sh shoulder at 1450  1379 w  1358 w   1334 s | 1479 vs shoulder at 1453 (rev.)  1422 m  1364 w, sh  1350 s, sh | 1625-1430 vr+m-s C=C stretching of aromatic rings  1450 – 1350 vr out-of-plane deformation of triazine ring  1360-1250s-m C(aromatic)-N stretching in primary aromatic amine | 1452 w, b  asym stretching of triazine ring  -C-C(Ν)- stretching of aromatic heterocyclic ring | 1452 s, sh |
| 1298 w-m, sh  1277 w, sh  1261 w, sh  1228 w  1167 w, sh  1136 m, sh  1107 w, sh  1088 m, sh shoulder at 1074 | 1299 m, sh  1273 w-m shoulder at 1263  1169 m 1135 vw  1107 w | 1290-990 s in-plane deformation of aromatic rings 1100 -1075 s C-O stretching (tetrahydrofurans) | 1071 w, b  in-plane ring deformation  C-O stretching of pyrrole | 1071 w, b |
| 1049 w, sh  1016 vs, br | 1016 w, sh shoulder at 1009 | 1290-990 s in-plane deformation of aromatic rings 1100 -1075 s C-O stretching (tetrahydrofurans)  1000-980 w Stretching of triazine ring | 1034 w, b  Η-C-C-H scissoring of pyrrole  C-O stretching (tetrahydrofurans)  Η-N-H rocking of amine | 1034 w, b |
| 1016 vs, br (rev.)  906 m, sh | 1016 m shoulder at 1009 (rev.)  906 w-m | 1290-990 s in-plane deformation of aromatic rings  1090-1000 s C-O stretching (primary alcohols)  1000-980 w stretching of triazine ring | 981 w, b  Η-C-C-H scissoring of pyrrole  stretching of triazine ring  Η-Ν-Η rocking of amine  C-O stretching (tetrahydrofurans) | 981 w, b |
| 906 m, sh (rev.)  860 m-s, sh  787 m-s, sh shoulder at 775  729 s  704 w shoulder at 678  607 w  577 w  540 w | 906 w-m (rev.)  780 w-m  717 s  705 s  639 w-m  620 w-m  581 w  544 w | 900-650 s stretching of aromatic rings  595 s deformation of furan ring | 694 vw  breathing of the whole molecule | 694 w, b |
| - | 433 w  396 w-m  358 w-m  328 w-m  252 w  211 w-m | 445-345 vr+w-m in-plane stretching of the bond aromatic ring – NH2 (in primary amines)  390-330 m C-O put of plane deformation in secondary alcohols | 259 s, sh | 259 vw |
| - | 153 w-m | - | 168 s, sh -ΟΗ deformation (secondary alcohols) and of furan ring | 168 vw |

**Table S5.** Atomic charge analysis of GS-441524 in water at B3LYP/6-311++G(d,p) level of theory.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Atom | Mulliken | CHelp | CHelpG | HLYGAt | MK |
| O1 | -0.226534 | -0.722152 | -0.775213 | -0.692774 | -0.710689 |
| O2 | -0.274071 | -0.669168 | -0.762110 | -0.705694 | -0.739593 |
| H3 | 0.312760 | 0.418991 | 0.465279 | 0.496170 | 0.487417 |
| O4 | -0.058908 | -0.610792 | -0.557800 | -0.359660 | -0.403893 |
| O5 | -0.381642 | -0.732038 | -0.716342 | -0.681570 | -0.700163 |
| H6 | 0.433436 | 0.326195 | 0.393466 | 0.416124 | 0.394827 |
| N7 | -0.392493 | -1.036757 | -1.047790 | -1.095260 | -1.090738 |
| H8 | 0.354506 | 0.417009 | 0.466467 | 0.479753 | 0.479980 |
| H9 | 0.318726 | 0.485569 | 0.474619 | 0.498538 | 0.493397 |
| N10 | 0.584084 | 0.591527 | 0.593161 | 1.032314 | 0.890515 |
| N11 | -0.239521 | -0.766739 | -0.859322 | -0.929738 | -0.903517 |
| N12 | -0.401223 | -0.516407 | -0.664993 | -0.810230 | -0.736113 |
| N13 | -0.282268 | -0.551425 | -0.557199 | -0.599054 | -0.594937 |
| C14 | -0.284529 | -0.131905 | -0.125168 | -0.110926 | -0.121292 |
| H15 | 0.214370 | 0.133539 | 0.142382 | 0.183987 | 0.175945 |
| C16 | -0.735631 | 0.121817 | 0.225621 | 0.145392 | 0.285203 |
| H17 | 0.275624 | 0.011439 | 0.015354 | 0.104627 | 0.045647 |
| C18 | 0.399941 | -0.413654 | -0.357929 | -0.708033 | -0.596944 |
| C19 | -0.211908 | 1.011575 | 0.991633 | 1.168021 | 1.121029 |
| C20 | -0.129412 | -0.090703 | -0.166922 | -0.235139 | -0.219469 |
| H21 | 0.202351 | 0.116247 | 0.145480 | 0.193271 | 0.188944 |
| C22 | -0.703041 | 0.645899 | 0.277703 | 0.094759 | 0.221478 |
| H23 | 0.186895 | -0.089358 | 0.008416 | 0.070911 | 0.024302 |
| H24 | 0.185752 | -0.117859 | 0.022381 | 0.102482 | 0.056714 |
| C25 | -0.565745 | 0.542448 | 0.449571 | 0.195118 | 0.221577 |
| H26 | 0.269021 | -0.079378 | -0.026618 | 0.102866 | 0.062753 |
| C27 | 0.829064 | 0.723880 | 0.463528 | -0.104253 | -0.017422 |
| C28 | -0.802811 | 0.371307 | 0.433173 | 0.686847 | 0.625542 |
| C29 | -0.310310 | -0.425515 | -0.275137 | -0.258788 | -0.257079 |
| C30 | 0.601499 | 0.083245 | 0.156278 | 0.034275 | 0.110746 |
| H31 | 0.287308 | 0.021997 | 0.047180 | 0.131497 | 0.090992 |
| C32 | 0.034425 | 0.513406 | 0.610194 | 0.601948 | 0.559808 |
| H33 | 0.234083 | 0.017701 | 0.042747 | 0.083724 | 0.089126 |
| H34 | 0.276202 | 0.400059 | 0.467909 | 0.468496 | 0.465909 |

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**Fig. S1.** Surface plot of the electrostatic potential of GS-441524 in water solvent at the B3LYP/6-311++G(d,p) level of theory.